Application No. 09/937,191
Filed: January 3, 2002
TC Art Unit: 1642
Confirmation No.: 6276

THE CLAIMS

1. (Currently Amended) Utilization of at least one aminopeptidase inhibitor for the production of a medicament used in the treatment of very early stages of tumor diseases ~~and/or immune diseases~~, wherein the treated tumor is a primary tumor, whereby the at least one aminopeptidase inhibitor causes blocking of polarization of invasive human or animal tumor cells ~~and/or immune cells~~ by modifying at least one surface protein CD13 as member of a protein network on the surface of the tumor cells ~~and/or immune cells~~, whereby the protein network comprises up to 30 surface proteins selected from ~~a~~ the group consisting of:

1. CD4	2. CD8	3. HLA-DR	4. HLA-DQ	5. CD3
6. CD26	7. CD38	8. CD45RA	9. CD16	10. CD57
11. CD56	12. CD7	13. CD54	14. CD58	15. CD138
16. CD13	17. CD62L	18. CD71	19. CD11b	20. CD36
21. CD29	22. CD49d	23. CD18	24. CD49f	25. CD19
26. CD2	27. CD20	28. CD10	29. CD44	30. CD80.

2. (Original) The utilization as claimed in claim 1 characterized in that

said at least one aminopeptidase inhibitor is an aminopeptidase inhibitor of the homophtalimide type and/or actinonin and/or bestatin, and/or an antibody, in particular a monoclonal antibody, against one of said surface proteins.

3. (Cancelled)

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4. (Currently Amended) The utilization as claimed in claim 1 characterized in that

for producing said medicament, at least one additional inhibitor is used ~~which~~ that inhibits at least one surface protein that is not an aminopeptidase.

5. (Currently Amended) The utilization as claimed in claim 1 characterized in that

said at least one aminopeptidase inhibitor and/or at least one additional inhibitor causes a modification of at least one surface protein of said tumor cells ~~and/or immune cells~~ which surface protein is responsible for adhesion to endothelial cells and/or extracellular structures, in particular organ-specific endothelial cells and/or organ-specific extracellular structures.

6. (Currently Amended) The utilization as claimed in claim 1 characterized in that

said at least one aminopeptidase inhibitor and/or at least one additional inhibitor will cause modification of the adhesive functions of endothelial cells.

7. (Original) The utilization as claimed in claim 1 characterized in that

the expression of at least one surface protein, in particular of an adhesion molecule, may be influenced by means of at least one aminopeptidase inhibitor and/or at least one additional inhibitor.

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8. (Currently Amended) A pharmaceutical preparation ~~which~~ that can be produced using at least one aminopeptidase inhibitor or a combination of at least one aminopeptidase inhibitor and at least one additional inhibitor as claimed in claim 1.

9. (Currently Amended) A method for identifying at least one aminopeptidase inhibitor ~~which~~ that causes blocking of polarization of invasive human or animal tumor cells of a primary tumor ~~and/or immune cells~~ created in the very early stages of tumor diseases, comprising:

a) detecting surface protein combinations of a protein network ~~which~~ that are on the surface of the untreated tumor cells ~~and/or immune cells~~, whereby the protein network comprises up to 30 surface proteins selected from ~~a~~ the group consisting of:

1. CD4	2. CD8	3. HLA-DR	4. HLA-DQ	5. CD3
6. CD26	7. CD38	8. CD45RA	9. CD16	10. CD57
11. CD56	12. CD7	13. CD54	14. CD58	15. CD138
16. CD13	17. CD62L	18. CD71	19. CD11b	20. CD36
21. CD29	22. CD49d	23. CD18	24. CD49f	25. CD19
26. CD2	27. CD20	28. CD10	29. CD44	30. CD80;

b) treating said or similar tumor cells ~~and/or immune cells~~ with at least one aminopeptidase inhibitor;

c) detecting said surface protein combinations of the protein network ~~which~~ that are on the surface of the treated tumor cells ~~and/or immune cells~~; and

d) comparing the surface protein combinations detected in steps a) and c), whereby the at least one aminopeptidase

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inhibitor, if there is a divergence of the surface protein combinations detected in step a) from the surface protein combinations detected in step c) in that there is at least one modification of surface protein CD13, will cause blocking of polarization of said tumor cells ~~and/or immune cells~~.

10. (Original) The method as claimed in claim 9 characterized in that

said method includes a further step, following step d), in which the at least one aminopeptidase inhibitor identified in step d) is added to at least one polarizing tumor cell and/or immune cell, and the further development of the at least one polarizing tumor cell and/or immune cell is detected.

11. (Currently Amended) The method as claimed in claim 9 characterized in that

said method includes a further step, following step d), in which any binding of the untreated tumor cells ~~and/or immune cells~~ to organ-specific endothelial cells and/or to organ-specific extracellular structures is detected, in which any binding of the tumor cells ~~and/or immune cells~~ treated with the at least one aminopeptidase inhibitor identified in step d) to the organ-specific endothelial cells and/or to the organ-specific extracellular structures is detected, and in which the detected bindings are compared.

12. (Currently Amended) A method for identifying at least one inhibitor ~~which~~ that in combination with at least one aminopeptidase inhibitor, will cause blocking of polarization of

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invasive human or animal tumor cells ~~and/or immune cells~~ of a primary tumor created in the very early stages of tumor diseases, comprising:

a) detecting surface protein combinations of a protein network ~~which~~ that are on the surface of the untreated tumor cells ~~and/or immune cells~~, whereby the protein network comprises up to 30 surface proteins selected from ~~a~~ the group consisting of

1. CD4	2. CD8	3. HLA-DR	4. HLA-DQ	5. CD3
6. CD26	7. CD38	8. CD45RA	9. CD16	10. CD57
11. CD56	12. CD7	13. CD54	14. CD58	15. CD138
16. CD13	17. CD62L	18. CD71	19. CD11b	20. CD36
21. CD29	22. CD49d	23. CD18	24. CD49f	25. CD19
26. CD2	27. CD20	28. CD10	29. CD44	30. CD80;

b) treating said or similar tumor cells ~~and/or immune cells~~ with at least one potential inhibitor ~~which~~ that is not directed against an aminopeptidase;

c) detecting the surface protein combinations of the protein network ~~which~~ that are on the surface of the treated tumor cells ~~and/or immune cells~~; and

d) comparing the surface protein combinations detected in steps a) and c), whereby the at least one inhibitor, if there is a divergence of the surface protein combinations detected in step a) from the surface protein combinations detected in step c) in that there is at least one modification of a surface protein, will be suitable for blocking polarization of said tumor cells ~~and/or immune cells~~.

13. (Currently Amended) The method as claimed in claim 12

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characterized in that

said or ~~the~~ similar tumor cells ~~and/or immune cells~~ are also treated with at least one aminopeptidase inhibitor in step b), with the combination of the at least one inhibitor and the at least one aminopeptidase inhibitor, if there is a divergence of the surface protein combinations detected in step a) from the surface protein combinations detected in step c) in that there is at least one modification of a surface protein CD13, will cause blocking of polarization of the tumor cells and/or immune cells.

14. (Previously Presented) The method as claimed in claim 12 characterized in that

said method includes a further step, following step d), in which the at least one aminopeptidase inhibitor identified in step d) or a combination of the at least one inhibitor identified in step d) and at least one aminopeptidase inhibitor is added to at least one polarizing tumor cell and/or immune cell, and the further development of the at least one polarizing tumor cell and/or immune cell is detected.

15. (Previously Presented) The method as claimed in claim 12 characterized in that

said method includes a further step, following step d), in which any binding of the untreated tumor cells and/or immune cells to organ-specific endothelial cells and/or to organ-specific extracellular structures is detected, in which any binding of the tumor cells and/or immune cells treated with the at least one inhibitor identified in step d) or with a combination of the at least one inhibitor identified in step d) and at least one

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aminopeptidase inhibitor to the organ-specific endothelial cells and/or to the organ-specific extracellular structures is detected, and in which the detected bindings are compared.

16. (Currently Amended) The utilization as claimed in claim 2 characterized in that

for producing said medicament, at least one additional inhibitor is used ~~which~~ that inhibits at least one surface protein that is not an aminopeptidase.

17. (Previously Presented) The method as claimed in claim 10 characterized in that

said method includes a further step, following step d), in which any binding of the untreated tumor cells and/or immune cells to organ-specific endothelial cells and/or to organ-specific extracellular structures is detected, in which any binding of the tumor cells and/or immune cells treated with the at least one aminopeptidase inhibitor identified in step d) to the organ-specific endothelial cells and/or to the organ-specific extracellular structures is detected, and in which the detected bindings are compared.

18. (Previously Presented) The method as claimed in claim 13 characterized in that

said method includes a further step, following step d), in which the at least one aminopeptidase inhibitor identified in step d) or a combination of the at least one inhibitor identified in step d) and at least one aminopeptidase inhibitor is added to at least one polarizing tumor cell and/or immune cell, and the

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further development of the at least one polarizing tumor cell and/or immune cell is detected.

19. (Previously Presented) The method as claimed in claim 13 characterized in that

said method includes a further step, following step d), in which any binding of the untreated tumor cells and/or immune cells to organ-specific endothelial cells and/or to organ-specific extracellular structures is detected, in which any binding of the tumor cells and/or immune cells treated with the at least one inhibitor identified in step d) or with a combination of the at least one inhibitor identified in step d) and at least one aminopeptidase inhibitor to the organ-specific endothelial cells and/or to the organ-specific extracellular structures is detected, and in which the detected bindings are compared.

20. (Previously Presented) The method as claimed in claim 14 characterized in that

said method includes a further step, following step d), in which any binding of the untreated tumor cells and/or immune cells to organ-specific endothelial cells and/or to organ-specific extracellular structures is detected, in which any binding of the tumor cells and/or immune cells treated with the at least one inhibitor identified in step d) or with a combination of the at least one inhibitor identified in step d) and at least one aminopeptidase inhibitor to the organ-specific endothelial cells and/or to the organ-specific extracellular structures is detected, and in which the detected bindings are compared.

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21. (Previously Presented) A pharmaceutical preparation which can be produced using at least one aminopeptidase inhibitor or a combination of at least one aminopeptidase inhibitor and at least one additional inhibitor as claimed in claim 2.

22. (Cancelled)

23. (Previously Presented) A pharmaceutical preparation which can be produced using at least one aminopeptidase inhibitor or a combination of at least one aminopeptidase inhibitor and at least one additional inhibitor as claimed in claim 4.

24. (Previously Presented) A pharmaceutical preparation which can be produced using at least one aminopeptidase inhibitor or a combination of at least one aminopeptidase inhibitor and at least one additional inhibitor as claimed in claim 5.

25. (Previously Presented) A pharmaceutical preparation which can be produced using at least one aminopeptidase inhibitor or a combination of at least one aminopeptidase inhibitor and at least one additional inhibitor as claimed in claim 6.

26. (Previously Presented) A pharmaceutical preparation which can be produced using at least one aminopeptidase inhibitor or a combination of at least one aminopeptidase inhibitor and at least one additional inhibitor as claimed in claim 7.

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